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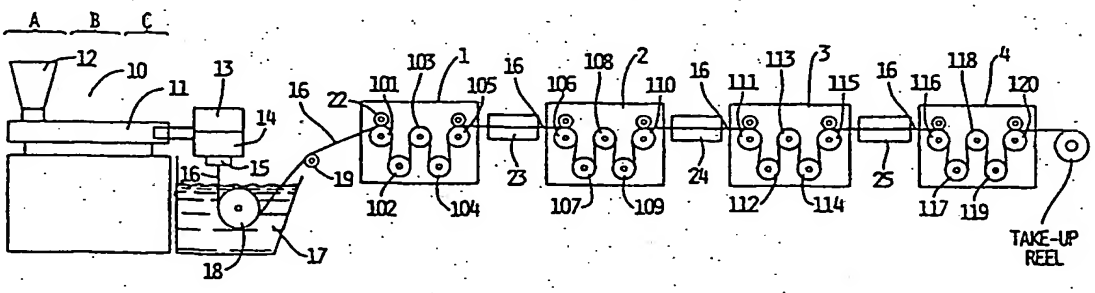

(57) Abstract

Synthetic absorbable medical devices made totally or in part from a random polymer comprising glycolide, lactide, trimethylene carbonate, and carpo-lactone, are provided. The polymer can be fabricated into monofilament (16) which exhibits physical characteristics equivalent to or superior than gut sutures.

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ABSORBABLE POLYMERS AND SURGICAL ARTICLES FABRICATED THEREFROM

TECHNICAL FIELD

Absorbable polymers of randomly polymerized glycolide, lactide, trimethylene carbonate, and caprolactone are described. Processes for making the polymers and surgical articles made totally or in part from such polymers, including sutures, are also described.

BACKGROUND

Bioabsorbable surgical devices made from copolymers derived from glycolide and epsilon-caprolactone are known in the art. Such bioabsorbable surgical devices include surgical sutures.

A desirable characteristic of a bioabsorbable suture is its ability to exhibit and maintain desired tensile properties for a predetermined time period followed by rapid absorption of the suture mass (hereinafter "mass loss".)

Synthetic absorbable sutures are known in the art. Absorbable multifilament sutures such as DEXON sutures (made from glycolide homopolymer and commercially available from Davis & Geck, Danbury, Connecticut), VICRYL sutures (made from a copolymer of glycolide and lactide and commercially available from Ethicon, Inc., Sommerville, New Jersey), and POLYSORB sutures (made from a copolymer of glycolide and lactide and commercially available from United States Surgical Corporation, Norwalk, Connecticut) are known in the industry as short term absorbable sutures. The classification short term absorbable sutures generally refers to surgical sutures which retain at least about 20 percent of their original strength at three weeks after implantation, with the suture mass being essentially absorbed in the body within about 60 to 90 days post implantation.

Long term absorbable sutures are generally classified as sutures capable of retaining at least about 20 percent of their original strength for six or more weeks after implantation, with the suture mass being essentially absorbed in the body within about 180 days post implantation. For example, PDS II sutures (commercially available from Ethicon, Inc., Sommerville, New Jersey), are synthetic absorbable monofilament sutures that reportedly retain at least about 20 to 30 percent of their original strength six weeks after implantation. However, PDS II reportedly exhibits minimal mass loss until 90 days after implantation with the suture mass being essentially absorbed in the body about 180 days after implantation. MAXON suture (commercially available from Davis & Geck, Danbury, Connecticut) is another absorbable synthetic monofilament that reportedly generally fits this absorption profile.

Recently, United States Surgical Corporation has introduced BIOSYN monofilament sutures which exhibit good flexibility, handling characteristics, knot strength and absorption characteristics similar to those of presently available short term absorbable multifilament sutures.

Another attempt to provide an acceptable synthetic absorbable monofilament sutures resulted in MONOCRYL, a suture fabricated from an absorbable block copolymer containg glycolide and epsilon-caprolactone, commercially available from Ethicon, Inc.

However, no synthetic absorbable monofilament sutures exist today which approximate the strength retention, mass loss, and modulus of sutures commonly referred to in the art as "catgut" or "gut" sutures. It is well known in the art that the term gut suture refers to a collagen based suture of any type or origin often fabricated from the mammalian intestines, such as the serosal layer of bovine intestines or the submucosal fibrous

layer of sheep intestines. Gut sutures exhibit the unique combination of two week strength retention and about 75 day mass loss while maintaining acceptable modulus and tensile strength; and thus are still widely used in gynecological surgery.

It would be advantageous to provide a synthetic absorbable suture which exhibits physical properties similar or superior to the gut suture.

U.S. Patent No. 4,700,704 to Jamiolkowski does teach that sutures can be fabricated from random copolymers of glycolide and epsilon-caprolactone, and more specifically from random copolymers containing from 20 to 35 weight percent epsilon-caprolactone and from 65 to 80 weight percent glycolide. Moreover, Jamiolkowski reports that sutures fabricated from glycolide/epsilon-caprolactone copolymers containing over 35% caprolactone are not orientable to a dimensionally stable fiber. Jamiolkowski further reports that some sutures fabricated from glycolide/epsilon-caprolactone copolymers containing 15% caprolactone are also not orientable to a dimensionally stable fiber. Furthermore, Jamiolkowski also reports the undesirable combination of low modulus and low tensile strength for the glycolide/epsilon-caprolactone copolymers which he was able to fabricate into sutures.

U.S. Patents 4,045,418 and 4,057,537 disclose random copolymers obtained by copolymerizing lactide and epsilon-caprolactone as well as terpolymers obtained by polymerizing lactide, epsilon-caprolactone, and glycolide. The copolymers as well as the terpolymers disclosed in U.S. Patents 4,045,418 and 4,057,537 have at least 60% by weight lactide. These copolymers have been described in the literature as having "one major drawback which has prevented their wide spread use. Although the copolymers can be literally interpreted to be 'bioabsorbable', the rate of absorption is so slow that it renders the copolymers practically useless for numerous medical

applications" (see U.S. Patent 5,468,253 at column 2, lines 24 et seq.). In fact, U.S. Patent 5,468,253 addresses this problem by disclosing medical devices formed from a random copolymer of: a) from about 30 to about 50 weight percent of epsilon-caprolactone, trimethylene carbonate, an ether lactone and combinations thereof, and b) the balance being substantially glycolide or para-trimethylene carbonate.

Therefore, it would be unexpected that medical devices such as sutures made from random copolymer of glycolide, epsilon-caprolactone, trimethylene carbonate, and lactide would provide the strength retention and mass loss characteristics approximating those of gut sutures while maintaining an acceptable modulus and tensile strength.

SUMMARY

It has now surprisingly been found that absorbable surgical articles formed from a random polymer of glycolide, caprolactone, trimethylene carbonate and lactide exhibit strength retention, mass loss and modulus similar to that of gut sutures. In one embodiment, the polymers used in forming surgical articles include between about 12 and about 17 weight percent of units derived from caprolactone, about 5 to about 8 weight percent of units derived from trimethylene carbonate, between about 68 and 75 weight percent of units derived from glycolide, and between about 5 to about 8 weight percent of units derived from lactide. In another embodiment, the polymers used in forming surgical articles include between about 12 and about 17 weight percent of units derived from caprolactone, about 1 to about 19 weight percent of units derived from trimethylene carbonate, between about 68 and 75 weight percent of units derived from glycolide, and between about 1 to about 19 weight percent of units derived from lactide.

In particularly useful embodiments, the random polymers can be spun into fibers. The fibers can be advantageously

fabricated into either monofilament or multifilament sutures having physical properties similar to those of gut sutures.

In addition, a process of making such synthetic absorbable monofilament sutures from the above described trimethylene carbonate/caprolactone/glycolide/lactide random polymers has been found. The process, for a given size suture, comprises the operations of extruding the random caprolactone/glycolide/trimethylene carbonate/lactide copolymer at an extrusion temperature of from about 140°C to about 180°C to provide a monofilament fiber, passing the solidified monofilament through water (or other suitable liquid medium) quench bath at a temperature of from about 15° C to about 25° C or through air (or other suitable gaseous medium) at from about 15°C to about 25°C, stretching the monofilament through a series of air ovens at an overall stretch ratio of from about 8:1 to about 11:1 to provide a stretched monofilament. In a particularly useful embodiment, the monofilament is stretched through three air ovens by four godet stations. The first air oven is maintained at about 25°C to about 35°C temperature, whereas the second air oven is heated to a temperature above the crystalization temperature of the glycolide/lactide/epsilon-caprolactone/trimethylene carbonate copolymer at about 80°C to about 100°C, and the third air oven is set at about 90°C to about 110°C. The draw ratio between the first and second godet station ranges between about 6:1 to about 8:1. The draw ratio between the second and third godet station ranges between about 12:1 to about 2.5:1. The draw ratio between the third and fourth godet station ranges between about 0.85:1 to about 1.05:1. The suture then may be annealed with or without relaxation at a temperature of from about 80°C to about 110°C to provide the finished suture.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1A is a schematic illustration of an apparatus which is suitable for manufacturing of monofilament sutures disclosed herein;

Fig. 1B is a modification of the apparatus shown in Fig. 1A which is particularily suitable for manufacturing monofilament sutures of smaller size; e.g. sizes 4/0 and smaller.

Fig. 2 is a perspective view of a suture attached to a needle.

Fig. 3A - 3C illustrate the formation of the knot which was employed in the loop pull test used in Table IV.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

It has been found that glycolide, epsilon-caprolactone, trimethylene carbonate, and lactide monomers can advantageously be combined to form a random polymer useful in forming surgical articles having strength retention, mass loss, and modulus characteristics similar to or superior to gut sutures.

The random polymer can be prepared using conventional techniques. For example, monomers can be dried, mixed in a reaction vessel with an initiator (either a single or multi-functional initiator) and a suitable polymerization catalyst and polymerized at temperatures from about 160°C to about 190°C for a period of time ranging from about 12 hours to about 48 hours.

The polymer has randomly combined repeating units derived from glycolide, lactide, trimethylene carbonate, and epsilon-caprolactone. In one embodiment, repeating units derived from glycolide comprise about 68 to about 75 weight percent of the polymer, while repeating units derived from lactide comprise about 5 to about 8 weight percent of the polymer, units derived from caprolactone comprise about 12 to

about 17 weight percent of the polymer, and units derived from trimethylene carbonate comprise about 5 to about 8 weight percent of the polymer. Polymers of trimethylene carbonate, caprolactone, glycolide, and lactide having an inherent viscosity of from about 1 to about 1.5 dl/g measured at 30°C and at a concentration of 0.25 g/dl in chloroform or HFIP may generally be used. In another embodiment, repeating units derived from glycolide comprise about 68 to about 75 weight percent of the polymer, while repeating units derived from lactide comprise about 1 to about 19 weight percent of the polymer, units derived from caprolactone comprise about 12 to about 17 weight percent of the polymer, and units derived from trimethylene carbonate comprise about 1 to about 19 weight percent of the polymer. Polymers of trimethylene carbonate, caprolactone, glycolide, and lactide having an inherent viscosity of from about 1 to about 1.5 dl/g measured at 30°C and at a concentration of 0.25 g/dl in chloroform or HFIP may generally be used.

The random polymers provided herein can be blended or copolymerized with other known absorbable polymers and/or coploymers derived from materials such as glycolide, lactide, caprolactone, trimethylene carbonate, dioxanone, alkylene oxides, absorbable amides and the like. It should be understood that the above list of materials with which the random copolymer can be either blended or copolymerized is provided for illustrative purposes and is not to be construed as limiting.

The random polymers can be formed into surgical articles using any known technique, such as, for example, extrusion, molding and/or solvent casting. The copolymers can be used alone, blended with other absorbable compositions, or in combination with non-absorbable components. A wide variety of surgical articles can be manufactured from the copolymers described herein. These include but are not limited to clips and other fasteners, staples, sutures, pins, screws, prosthetic

devices, wound dressings, drug delivery devices, anastomosis rings, and other implantable devices. Fibers made from the copolymers can be knitted, woven or made into non-woven materials with other fibers, either absorbable or nonabsorbable to form fabrics, such as meshes and felts. Compositions including these random copolymers can also be used as an absorbable coating for surgical devices. Preferably, however, the polymers are spun into fibers to be used in making sutures.

Multifilament sutures of the present invention may be made by methods known in the art. Braid constructions such as those disclosed and claimed in U.S. Patent No.'s 5,059,213 and 5,019,093 are suitable for the multifilament suture of the present invention.

Fig. 1A substantially illustrates the extruding, quenching and stretching operations of the monofilament manufacturing operation herein. Extruder unit 10 is of a known or conventional type and is equipped with controls for regulating the temperature of barrel 11 in various zones thereof, e.g., progressively higher temperatures in three consecutive zones A, B and C along the length of the barrel. Pellets or powder of resins of the present invention are introduced to the extruder through hopper 12. Any of the above described polymers which are useful for the formation of fibers can be used herein.

Motor-driven metering pump 13 delivers melt extruded resin at a constant rate to spin pack 14 and thereafter through spinneret 15 possessing one or more orifices of desired diameter to provide a molten monofilament 16 which then enters quench bath 17, e.g., containing water, where the monofilament solidifies. The distance monofilament 16 travels after emerging from spinneret 15 to the point where it enters quench bath 17, i.e., the air gap, can vary and can advantageously be from about 1 to about 5cm and preferably from about 2 to about

3cm. If desired, a chimney (not shown), or shield, can be provided to isolate monofilament 16 from contact with air currents which might otherwise affect the cooling of the monofilament in an unpredictable manner. In general, barrel zone A of the extruder can be maintained at a temperature of from about 140°C to 160°C, zone B at from about 140°C to 165°C and zone C at from about 145°C to about 170°C. Additional temperature parameters include: metering pump block 13 at from about 140°C to about 170°C, spinneret 15 at from about 150°C to about 180°C and quench bath at from about 15°C to about 25°C.

Monofilament 16 is passed through quench bath 17 around driven roller 18 and over idle roller 19. Optionally, a wiper (not shown) may remove excess water from the monofilament as it is removed from quench bath 17. On exiting the quench bath the monofilament is passed through first godet station 1, which is equiped with five individual godets, i.e. godets 101, 102, 103, 104 and 105. Upon entering godet station 1, monofilament 16 is wrapped around a first godet 101 provided with nip roll 22 to prevent slippage which might otherwise result from the subsequent stretching operation; and subsequently passed over godet 101, under godet 102, over godet 103, under godet 104, and over godet 105 to godet station 2, containing godets 106, 107, 108, 109, and 110, where it is wrapped over godet 106, under godet 107, over godet 108, under godet 109, and over godet 110. Monofilament 16 passing from godet station 1 to godet station 2 is drawn through air oven 23 at a temperature ranging form about 25°C to about 35°C by the godets of godet station 2 which rotate at speeds faster than the speed of the godet station 1 to provide the desired draw ratio, which is from about 6:1 to about 8:1 and preferably from about 6.5:1 to about 7.5:1, to effect the molecular orientation of the copolymer from which it is fabricated and thereby increase its tensile strength.

Following the initial draw at about 25°C to about 35°C temperature, monofilament 16 is then subjected to a second and a third drawing operation. Monofilament 16 is

subsequently drawn from godet 110 through air oven 24, which is maintained at from about 80°C to about 100°C, to godet station 3 containing godets 111, 112, 113, 114, and 115 where it is wrapped over godet 111, under godet 112, over godet 113, under godet 114, and over godet 115. Godet station 3 spins faster than godet station 2 to provide the desired draw ratio, which is from about 1.2:1 to about 2.5:1. Monofilament 16 is then drawn from godet 115 through air oven 25, which is maintained at from about 90°C to about 110°C, by godet station 4, containing godets 116, 117 118, 119, and 120 where it is wrapped over godet 116, under godet 117, over godet 118, under godet 119, and over godet 120. Godet station 4 spins at a variable rate, (preferably faster than godet station 3) to provide the desired draw ratio, which is from about 0.85:1 to about 1.05:1. It should be understood that the godet arrangements in each of godet stations 1, 2, 3, and 4, respectively should not be limited to the above described arrangement and that each godet station may have any suitable godet arrangement.

In an alternative operation for sutures for smaller size sutures, e.g. sizes 4/0 to 8/0, as showm in Fig. 1B monofilament 16 is only passed through godet stations 1 and 2 and not subjected to any further stetching operations.

Annealing of the suture also may be accomplished with or without shrinkage of the suture. In carrying out the annealing operation, the desired length of suture may be wound around a creel and the creel placed in a heating cabinet under nitrogen flow maintained at the desired temperature, e.g. about 80°C to about 110°C, as described in U.S. Patent No. 3,630,205. After a suitable period of residency in the heating cabinet, e.g., for up to about 18 hours or so, the suture will have undergone essentially no shrinkage. As shown in U.S. Patent No. 3,630,205, the creel may be rotated within the heating cabinet in order to insure uniform heating of the monofilament or the cabinet may be of the circulating hot air type in which case uniform heating of the monofilament will be achieved without the

need to rotate the creel. Thereafter, the creel with its annealed suture is removed from the heating cabinet and when returned to room temperature, the suture is removed from the creel, conveniently by cutting the wound monofilament at opposite ends of the creel. The annealed sutures, optionally attached to surgical needles, are then ready to be packaged and sterilized.

Alternatively, the suture may be annealed on line with or without relaxation. For relaxation, the fourth godet station rotates at a slower speed than the third godet station thus relieving tension on the filament.

The suture disclosed herein, suture 101, may be attached to a surgical needle 100 as shown in Fig. 2 by methods well known in the art. Wounds may be sutured by passing the needled suture through tissue to create wound closure. The needle preferably is then removed from the suture and the suture tied.

One or more medico-surgically useful substances can be incorporated into the presently disclosed polymers and surgical articles, e.g., those medico-surgically useful substances which accelerate or beneficially modify the healing process when particles are applied to a surgical repair site. So, for example, the suture can carry a therapeutic agent which will be deposited at the repair site. The therapeutic agent can be chosen for its antimicrobial properties, capability for promoting repair or reconstruction and/or new tissue growth. Antimicrobial agents such as broad spectrum antibiotic (gentamycin sulfate, erythromycin or derivatized glycopeptides) which are slowly released into the tissue can be applied in this manner to aid in combating clinical and sub-clinical infections in a tissue repair site. To promote repair and/or tissue growth, one or several growth promoting factors can be introduced into the sutures, e.g., fibroblast growth factor,

bone growth factor, epidermal growth factor, platelet derived growth factor, macrophage derived growth factor, alveolar derived growth factor, monocyte derived growth factor, magainin, and so forth. Some therapeutic indications are: glycerol with tissue or kidney plasminogen activator to cause thrombosis, superoxide dimutase to scavenge tissue damaging free radicals, tumor necrosis factor for cancer therapy or colony stimulating factor and interferon, interleukin-2 or other lymphokine to enhance the immune system.

It is contemplated that it may be desirable to dye the sutures in order to increase visibility of the suture in the surgical field. Dyes known to be suitable for incorporation in sutures can be used. Such dyes include but are not limited to carbon black, bone black, D&C Green No. 6, and D&C Violet No. 2 as described in the handbook of U.S. Colorants for Food, Drugs and Cosmetics by Daniel M. Marrion (1979). Preferably, sutures in accordance with the invention are dyed by adding up to about a few percent and preferably about 0.2% dye, such as D&C Violet No. 2 to the resin prior to extrusion, although addition of the dye during polymerization is also suitable.

In order that those skilled in the art may be better able to practice the compositions and methods described herein, the following examples are given as an illustration of the preparation of random polymers as well as of the preparation and superior characteristics of sutures made from the random copolymers. It should be noted that the invention is not limited to the specific details embodied in the examples and further that all ratios or parts recited are by weight, unless otherwise indicated.

EXAMPLE 1

Dry glycolide (4140 grams), dry l-lactide (420 grams), trimethylene carbonate (420grams) and distilled epsilon-caprolactone (1020 grams) were added to a reactor along with 0.72 grams of distilled stannous octoate and 1.2 grams of distilled diethylene glycol (DEG). The mixture was dried for about 22.5 hours with agitation under flow of nitrogen. The reactor temperature was then set at 100°C. When the temperature of the reaction vessel reached 100°C, the temperature was maintained for about 15 minutes. Then the temperature of the reaction vessel was raised to 150°C and then the reaction vessel heated for about an additional 15 minutes. The temperature of the reactants was then raised to about 180°C and polymerization conducted with stirring under a nitrogen atmosphere for about 18 hours.

The reaction product is then isolated, comminuted, and treated to remove residual reactants using known techniques. The treatment to remove residual reactants occurred at 90°C for 48 hours under vacuum. NMR analysis, using a commercially available Bruker NMR, model number DPX-300, revealed the resultant polymer contained 7.25 weight percent lactide, 15.87 weight percent caprolactone, 6.84 weight percent trimethylene carbonate, and 70.04 weight percent glycolide.

EXAMPLE 2

Dry glycolide (4260 grams), dry l-lactide (420 grams), trimethylene carbonate (420 grams) and distilled epsilon-caprolactone (900 grams) were added to a reactor along with 0.72 grams of distilled stannous octoate and 1.2 grams of distilled diethylene glycol (DEG). The mixture was dried for about 6 hours with agitation under flow of nitrogen. The reactor temperature was then set at 100°C. When the temperature of the reaction vessel reached 100°C, the temperature was maintained for about 15 minutes. Then the temperature of the reaction vessel was raised to 150°C and then the reaction vessel heated

for about an additional 15 minutes. The temperature of the reactants was then raised to about 180°C and polymerization conducted with stirring under a nitrogen atmosphere for about 18 hours.

The reaction product is then isolated, comminuted, and treated to remove residual reactants using known techniques. The treatment to remove residual reactants occurred at 90°C for 48 hours under vacuum. NMR analysis, using a commercially available Bruker NMR, model number DPX-300, revealed the resultant polymer contained 7.2 weight percent lactide, 13.9 weight percent caprolactone, 6.8 weight percent trimethylene carbonate, and 72.1 weight percent glycolide.

TABLE I

CONDITIONS OF MANUFACTURING VARIOUS SIZES OF MONOFILAMENT OF THE PRESENT INVENTION

Example	1	2
Suture Size	3/0	3/0
Process Conditions	Extrusion	
extruder screw, rpm	4.4	3.0
pump, rpm	12.9	8.4
driven roller, mpm	2.5	1.9
barrel temp., °C, zone A	140	140
barrel temp., °C, zone B	143	145
barrel temp., °C, zone C	146	147
clamp temp., °C,	153	155
adapter temp., °C	153	157
spinneret temp., °C	153	160

block temp., °C	153	160
barrel melt temp., °C	152	154
pump melt temp., °C	157	163
spinneret melt temp., °C	159	166
barrel pressure, psi	550	540
pump pressure, psi	500	500
spinneret pressure, psi	730	580
pump size, cc per revolution	0.16	0.16
diameter of spinneret, orifices, mm	1.2	1.2
no. of spinneret orifices	1	1
quench bath temp., °C	27	25

Stretching (Orienting) Operation

Example	1	2
draw bath temp., °C	N/A	N/A
first godet station, mpm	2.7	2.0
	1	2
second godet, mpm	17.7	13.3
third godet station, mpm	24.9	17.5
fourth godet station, mpm	25.2	15.6
first oven temp, °C	29	31
second oven temp, °C	94	96
third oven temp, °C	90	100
overall draw ratio	9.33:1	8.75:1
Relaxation	N/A	11%

Annealing Operation

Example	1	2
annealing temp., °C	90	90
time (hrs.)	6	6

The physical properties of the sutures and the procedures employed for their measurement are set forth in Table II as follows:

TABLE II

PROCEDURES FOR MEASURING PHYSICAL PROPERTIES OF MONOFILAMENT SUTURES OF THE PRESENT INVENTION

Physical Property	Test Procedure
knot-pull strength, kg	U.S.P. XXI, tensile strength, sutures (881)
straight-pull strength, kg	ASTM D-2256, Instron Corporatio
elongation, %	ASTM D-2256
tensile strength, kg/mm^2	ASTM D-2256, Instron Corporatio Series IX Automated Materials Testing System 1.03A
Young's Modulus	Instron Merlin Software versio 2000 Series IX calculation 18.5 (commercially available from Instron Corporation)

Table III below sets forth the physical properties of the size 3/0 suture of the present invention.

TABLE III

Physical Property	Example 1	Example 2
diameter (mm)	0.325	0.32
knot-pull strength (kg)	2.58	3.15
Young's Modulus (kpsi)	229	453
Elongation %	26	29
Tensile Strength (kpsi)	88.3	103.6

As the data in Tables III illustrates, the suture made of the copolymer provided herein shows a desired physical properties, such as modulus and tensile strength.

IN VITRO STRENGTH RETENTION

Monofilament sutures manufactured in accordance with the above described process using the copolymer of Example 1 were tested for in vitro strength retention. In vitro loop-pull strength retention is indicative of in vivo strength retention. The in vitro strength retention of the suture was tested as follows:

To simulate in vivo conditions, the suture samples were stored in a container filled with Sorenson's buffer solution at 37°C. After various periods of time, the suture samples were then removed from the container to test their loop-pull strength as follows. A knotted loop was formed in a test suture in three steps as shown in FIGS. 3A - 3C. As shown in step 1 of FIG 3A , each suture was given a double throw (left over right) around a 2 cm diameter cylinder. In Step 2, the free ends of the suture were set in a single throw (right over left) onto the initial throw of step 1. Finally, in step 3, another double throw (left over right) was set onto the single throw of Step 2 to complete the knot. The free ends of the suture were cut to approximately 0.5 inches and the loop was carefully eased from the cylinder.

Testing of the loop was carried out using an Instron Tensile Tester Model No. 4307 (commercially available from Instron Corporation, Canton, Massachusetts), operated with a crosshead speed of 51 mm/min and equipped with flat grips, each having a pin over which the loop is positioned.

The results of the tests are presented in Table IV hereinbelow. In the strength retention data reported in Table IV, T_n represents the time elapsed in weeks since the sample was placed in the solution, with n representing the number of weeks.

TABLE IV

COMPOSITION	PERCENTAGE OF IN VITRO STRENGTH RETAINED		
	T_1	T_2	T_3
EXAMPLE 1	73.7	15.7	0
EXAMPLE 2	83.9	18.8	0
Monocryl	58	26	3

IN VITRO MASS LOSS

Monofilament sutures manufactured in accordance with the above described process using the polymer of Examples 1-3 were tested for in vitro mass retention. In vitro mass retention is indicative of in vivo mass retention. The in vitro strength retention of the suture was tested as follows:

To simulate in vivo conditions, the suture samples were weighed and stored in a fritted microencapsulation thimble (commercially available from Chemglass, Inc., Vineland, New Jersey), which was placed in a scintillation vial filled with Sorenson's buffer solution. The scintillation vials were then placed in a water bath at 80°C. After various periods of time, the microextraction thimbles containing the suture samples were then removed from the scintillation vial, vacuum filtered, rinsed with distilled water, vacuum filtered, and dried for about 6 hours at about 40°C under vacuum and subsequently the suture and thimble were weighed. The weight of the suture remaining was calculated by subtracting the weight of the thimble from the weight of the thimble containing the remaining suture. The percentage of the suture retained was calculated by dividing the weight of the remaining suture by the original weight of the suture and multiplying the result by 100.

The results of the tests are presented in Table V hereinbelow. In the mass retention data reported in Table V, T_n represents the time elapsed in hours since the sample was placed in the solution, with n representing the number of hours. It is well known in the art that one hour of immersion in the container filled with Sorenson's buffer solution at 80°C approximates about one day of in vivo mass loss. For comparison purposes, the same tests were conducted on Monocryl sutures.

All comparative tests were performed on size 3/0 sutures.

TABLE V

	PERCENTAGE OF IN VITRO MASS RETAINED						
	T_1	T_2	T_3	T_4	T_6	T_8	T_{10}
Time (hr)	8	24	32	48	72	96	120
EXAMPLE 1	92.8	58.34	42.14	29.09	21.91	18.01	13.58
EXAMPLE 2	92.11	59.62	45.08	32.96	25.18	20.62	16.26
Monocryl	94.86	74.79	66.83	47.95	35.31	27.32	17.37

It will be understood that various modifications may be made to the embodiments disclosed herein. Therefore, the above description should not be construed as limiting, but merely as exemplifications of preferred embodiments. Those skilled in the art will envision other modifications within the scope and spirit of the claims appended hereto.

WHAT IS CLAIMED IS:

1. A medical device fabricated totally or in part from a random polymer comprising from about 68 to about 75 weight percent glycolide, about 12 to about 17 weight percent epsilon-caprolactone, about 1 to about 19 weight percent trimethylene carbonate, and about 1 to about 19 weight percent lactide.

2. The medical device of claim 1 wherein the device is a surgical suture.

3. The suture of claim 2 wherein the random polymer comprises about 70 weight percent glycolide, about 16 weight percent caprolactone, and about 7 weight percent lactide, and about 7 weight percent trimethylene carbonate.

4. The suture of claim 2 wherein the suture exhibits two week strength retention of about 15% to about 19%, as measured in Sorenson's buffer solution at 37°C.

5. The suture of claim 2 wherein the suture exhibits a mass retention of about 13% to about 17% as measured after 120 hours in Sorenson's buffer solution at 80°C.

6. The suture of claim 2 wherein the suture exhibits a modulus ranging from about 200 kpsi to about 500 kpsi.

7. The suture of claim 2 wherein the suture exhibits a knot pull strength of about 2.0 to about 3.5kg for size 3/0.

8. The suture of claim 2 wherein the suture is a size 3/0 suture exhibiting a modulus of about 230 kpsi.

9. The suture of claim 1 wherein the suture is a size 3/0 suture exhibiting a knot pull strength of about 2.6 kg.

10. The suture of claim 1 wherein the suture is a size 3/0 suture exhibiting a tensile strength of about 90 kpsi.

11. The suture of claim 1 wherein the suture is a size 3/0 suture exhibiting the following characteristics:

modulus	about 200 to about 500 kpsi
knot pull strength	about 2 to about 3.5 kg
tensile strength	about 80 to about 110 kpsi.

12. The medical device of claim 1 comprising a medico-surgically useful substance.

13. The suture of claim 1 wherein the random polymer possesses an inherent viscosity of about 0.8 to about 1.6 dl/g at 30°C and at a concentration of 0.25g/dl in HFIP.

14. The suture of claim 1 wherein the suture is a size 3/0 suture and exhibits a mass retention of about 59% after 24 hours in Sorenson's buffer solution at 80°C.

15. The suture of claim 1 wherein the suture is a size 3/0 suture and retains a mass retention of about 29% to about 33% after 48 hours in Sorenson's buffer solution at 80°C.

16. The suture of claim 1 wherein the suture is a size 3/0 suture and retains a mass of about 13% to about 16% after 120 hours in Sorenson's buffer solution at 80°C.

17. The medical device of claim 1 wherein the device is a staple, clip, other fastener, pin, screw, prosthetic device, mesh, or felt.

18. The medical device of claim 1 wherein the random polymer is blended with at least one another bioabsorbable composition.

19. The medical device of claim 18 wherein the other bioabsorbable composition comprises units selected from the group consisting essentially of glycolide, lactide, trimethylene carbonate, dioxanone, alkylene oxide, bioabsorbable amides and combinations thereof.

20. The medical device of claim 1 wherein the random copolymer is copolymerized with one other bioabsorbable composition.

21. The medical device of claim 20 wherein the other bioabsorbable composition comprises units selected from the group consisting essentially of glycolide, lactide, trimethylene carbonate, dioxanone, alkylene oxide, bioabsorbable amides and combinations thereof.

22. A method of suturing a wound comprising:

a. providing a suture fabricated from a random polymer comprising from about 68 to about 75 weight percent glycolide, about 12 to about 17 weight percent epsilon-caprolactone, about 1 to about 19 weight percent trimethylene carbonate, and about 1 to about 19 weight percent lactide.and

b. passing said needled suture through tissue to create wound closure.

23. A process for manufacturing a monofilament suture from a resin of a random copolymer, the random polymer comprising from about 68 to about 75 weight percent glycolide, about 12 to about 17 weight percent epsilon-caprolactone, about 1 to about 19 weight percent trimethylene carbonate, and about 1 to about 19 weight percent lactide., which comprises the operations of:

a. extruding said resin at an extrusion temperature of from about 140°C to about 180°C to provide a monofilament;

b. stretching the solidified monofilament at a stretch ratio of from about 8:1 to about 11:1 to provide a stretched monofilament.

24. The process of claim 21 further comprising the steps of:

a. annealing said stretched monofilament at a temperature of from about 80°C to about 110°C to provide a finished suture.

25. A method of manufacturing a monofilament suture from a resin of a random copolymer, the random copolymer comprising caprolactone, trimethylene carbonate, lactide, and glycolide, which comprises:

a) extruding the copolymer to provide a molten monofilament;

b) quenching the molten monofilament to provide a solidified monfilament;

c) drawing the solidified monofilament through an air oven maintained at a temperature of about 25°C to about 35°C at a draw ratio of about 6:1 to about 8:1;

d) drawing the monofilament through an air oven maintained at a temperature of about 80°C to about 100°C at a draw ratio of about 1.2:1 to about 2.5:1;

e) drawing the monofilament through an air oven maintained at a temperature of about 90°C to about 110°C at a draw ratio of about 0.85:1 to about 1.05:1; and

f) annealing the monofilament.

26. The method of claim 25 wherein the random copolymer comprises from about 68 about 75 weight percent glycolide, about 12 to about 17 weight percent epsilon-caprolactone, about 1 to about 19 weight percent trimethylene carbonate, and about 1 to about 19 weight percent lactide.

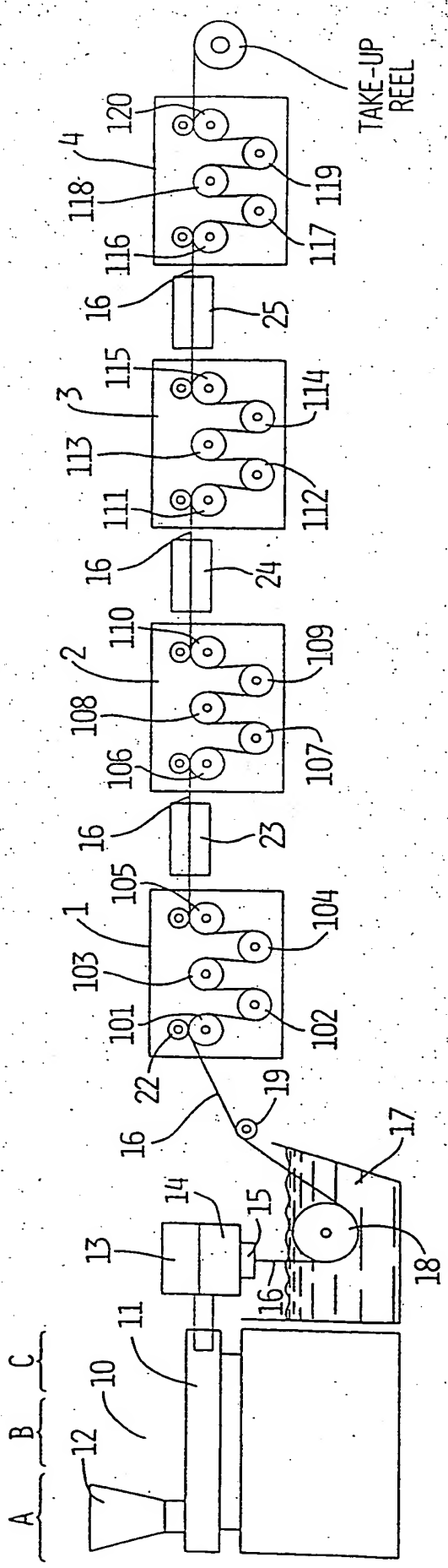
TAKE-UP REEL
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FIG_1

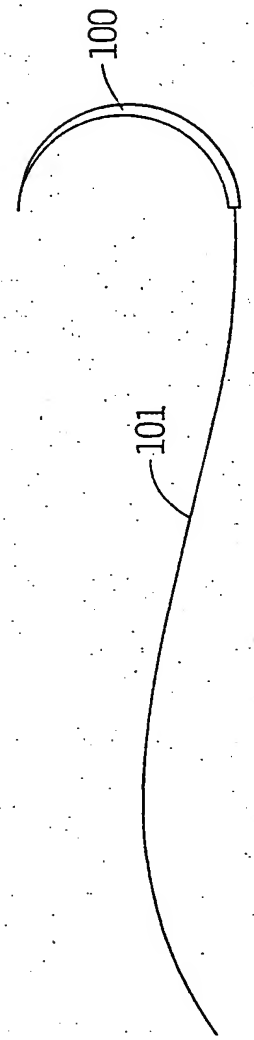
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FIG_2

FIG_3A

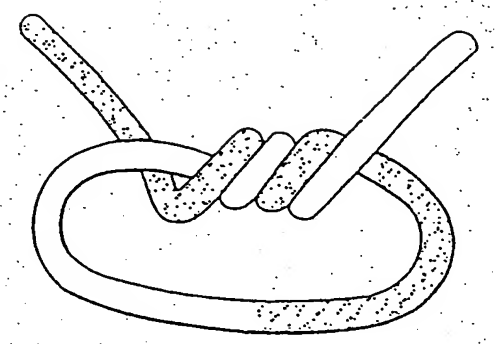


FIG_3B

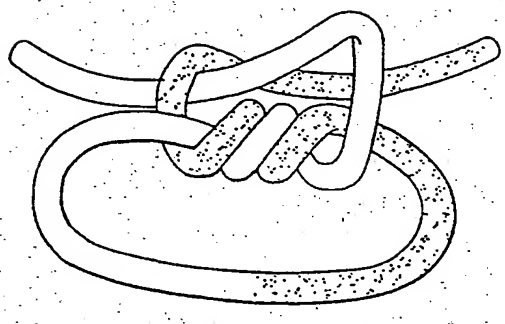
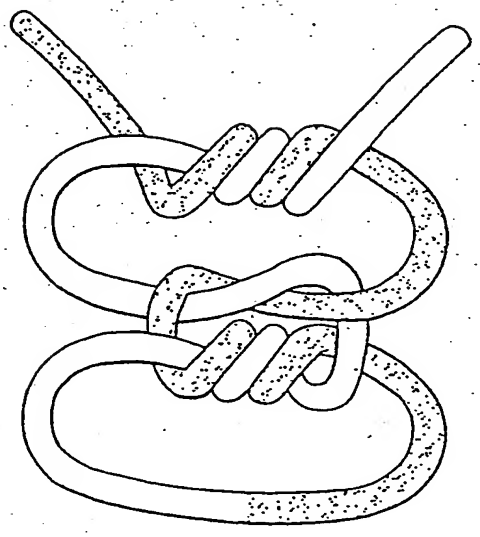


FIG_3C



INTERNATIONAL SEARCH REPORT

International application No.
PCT/US99/24404

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A61B 17/04
US Cl. :606/230

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 606/229-231

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5,236,444 A (MUTH et al.) 17 August 1993, entire document.	1-26
A,P	US 5,925,065 A (TOTAKURA et al.) 20 July 1999, entire document.	1-26

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

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